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Molluscum Contagiosum in Children: Primary care consultation rates and associations with atopic eczema.

A retrospective longitudinal study.

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Abstract

Background: Molluscum contagiosum (MC) is a common skin condition in children. The consultation rates and current management in primary care, and how these have changed over time, are poorly described. An association between presence of atopic eczema (AE) and MC has been shown, but the subsequent risk of developing MC in children with a diagnosis of AE is not known.

Aim: Describe the consultation rate and management of MC in general practice in the UK over time, and test the hypothesis that a history of AE increases the risk of developing MC in childhood.

Design, setting and Methods: Two studies are reported. A retrospective longitudinal study of MC cases and an age-sex matched case-cohort study of AE cases, both datasets being held within the UK Clinical Practice Research Datalink (CPRD) from 2004-2013.

Results: The rate of MC consultations in primary care for children aged 0 to 14 years is 9.4 per 1,000 (95% CI 9.3 to 9.4). The greatest rate of consultations for both genders is in children aged 1 to 4 and 5 to 9 years (12.8 and 13.7 per 1,000 respectively). Consultation rates for MC have declined from 2004 to 2013 by 50%. We found children were more likely to have an MC consultation if they had previously consulted to a general practitioner with AE (OR:1.13 (95% CI 1.10 to 1.16) $P<0.005$).

Conclusions: Consultations for MC in primary care are common, especially in 1-9 year olds, but declined significantly during the decade under study. A primary care diagnosis of AE is associated with an increased risk of a subsequent primary care diagnosis of MC.

Introduction

Molluscum Contagiosum (MC) is a common skin condition that predominately affects children (1) and is one of the 50 most prevalent diseases globally (2). MC typically presents as one or more umbilicated, smooth, flesh-coloured, domed shaped lesions (3), and is usually diagnosed on clinical examination by a general practitioner or dermatologist (4). The condition can impact on quality of life, with around one in 10 children experiencing a substantial effect on their quality of life (5).

A study in England and Wales described consultation rates during 2006 (6), but there have been no recent studies and no studies exploring recent changes over time (7). Furthermore, no studies have described primary care management, including prescribing and referrals to secondary care (8).

Atopic eczema (AE) has been found to be common in children with MC (9-13) and the prevalence of AE is higher in children with MC than in the general population (14, 15). However, most studies describing this association have been based in speciality dermatology clinics (12), and have not explored the temporal relationship between the two conditions. It is not clear whether this relationship holds for children with AE or MC in the community, or whether there is a time-dependent direction (i.e. children with AE are more likely to develop MC).

We aimed to describe consultation rates of MC in general practice in the UK, and test the hypothesis that that a diagnosis of AE increases the subsequent risk of developing MC in children.

Methods

Study Design and data source

Two analyses drawn for CPRD data are reported: a retrospective longitudinal analysis of MC cases presenting to General Practice in the UK, and an age-sex matched case-cohort analysis to examine the likelihood of developing MC in children who have previously presented to general practices with atopic eczema (AE). MC and AE were defined as having a Read-code for either condition (supplementary table 1) if aged between 0 to 14 years at time of consultation between 2004 and 2013 (inclusive). Controls for the case-cohort analysis were selected at random within age-sex strata at a ratio of 1:1. Patients were excluded from the population pool before the controls were selected if they had a Read-code of AE, 'transferred out of practice', or died during the study period. All data were extracted from the UK Clinical Practice Research Datalink (CPRD) which is a primary care database of anonymised patient records, representing approximately 6% of the UK population. CPRD contains data on over 4 million active patients from over 500 primary care practices across the UK (16). The base population for both analyses was all CPRD UK registered patients aged 0 to 14 years, per year for the period 2004 to 2013. Patients must have been registered in the practice during the year to be included within the denominator population for that year. Only data from GP practices that were defined as "up to standard" by the CPRD standard definition were included within the study. The data extraction process is shown in Figure 1.

Statistical Analysis

For the retrospective cohort analysis, the consultation rate for MC was calculated using age-specific number of consultations divided by the total person-years in each age group from the CPRD population. Consultation rates were produced by age and year to produce annual

trends. Prescription medications by BNF chapter heading, patient episodes and referrals to dermatology specialty care were described. The age groups used in the analysis were under 1, 1 to 4, 5 to 9, and 10 to 14 years.

Matched cohort study

For the matched-cohort analysis logistic regression analysis was used to determine odds ratios for the association between 'exposure' to AE and the risk of an MC outcome. Baseline exposure to AE was defined as a thirty day AE free 'wash-in' period where there are no consultations for AE prior to an initial MC consultation. Multivariate analyses were also performed to establish associations of developing MC within the group of patients with AE for age, corticosteroid strength and eczema diagnosis (primary and secondary diagnosis, as identified by Read-codes – Supplementary table 1).

Significance was assumed at the 5% level, and 95% confidence intervals are reported. Analysis was performed in STATA v12.

Results

Retrospective cohort analysis

During the period 2004-13, there were 116,234 consultations for MC in 89,015 (44,995 males: 50.6%) patients within the CPRD database (Figure 1).

Consultation rates for MC

Age and Gender

The highest consultation rates were in the 1 to 4 and 5 to 9 age groups for both males and females. Consultation rates for males were marginally higher in the 1 to 4 year age group

(13.1 per 1,000) than the 5 to 9 year group (13.0 per 1,000), however for females the greatest rate of consultations was in the 5 to 9 year age group (13.9 and 13.0 per 1,000 in 5 to 9 and 1 to 4 age group respectively) (Table 1).

Trends

Consultations for MC have been steadily declining from 2004 to 2013. Rates for males and female have declined by 50.0% over the 10 year period. Decreases in consultation rates were highest for children within the 1 to 4 and 5 to 9 age groups (Figure 2). Rates for children aged 10 to 14 years declined during 2004 to 2008 and remained constant from 2008 to 2013. There was little variation in the rate of consultations for children aged less than 1 year over the 10-year period.

Consultations per patient

Most patients consulting for MC did so once (77.3%), 17.6% had two consultations for MC, and a small proportion (~5%) presented on 3 or more occasions over the 10-year period. The time between MC consultations varied, 89.5% of patients who consulted more than once (n:20,195) did so within 1 year of their initial consultation. Where data are presented as patient episodes, assuming a singular episode of MC will have multiple consultations within 180 days, 90.4% of children had one episode of MC, 9.3% two, and 0.3% three or more.

Referral to secondary care

There were 733 (0.8% of all consultations) referrals to a secondary care dermatology department for children presenting with MC. The greatest referral rate was in those aged 10 to 14 years (9.9 per 1,000 MC consultations). The rate of referrals from 2004 to 2013

reduced significantly by 74.4% during the 10 year period. Of the patients who were referred to a secondary care setting, 73.4% had consulted 2 or more times.

Prescribed medications

41,489 (46.6%) of patients received a treatment during a consultation for MC. 41,419 (99.8%) during a single episode (MC consultation within 90 days of previous) and 70 (2.0%) during a subsequent episode.

Of the 41,489 patients who were prescribed a treatment during a consultation with a code for MC, a total of 71,404 treatments were prescribed. The average number of items per patient was 1.7. Treatments prescribed in over 1% of cases are listed in Table 2 by BNF sub-section headings.

Matched cohort analysis

MC and atopic eczema consultations

During the period 2004-13 there were 792,282 consultations identified with an AE Read-code, representing 377,885 individual patients (Figure 1).

58.9% of children consulted once for AE, 19.4% did so twice, and one patient consulted 105 times during the 10 year period (Table 3). The mean number of consultations per patient was 2.5.

In children who consulted for both AE and MC, around two thirds (65.2%) of initial AE consultations were more than 30 days prior to their first consultation for MC (Table 3).

In the univariate model, children diagnosed with AE were more likely to have a future MC consultation during childhood than controls (OR:1.13 (95% CI 1.10 to 1.16) $P<0.005$) (Table 4a).

Corticosteroid potency and type of AE diagnosis did not influence the likelihood of an MC diagnosis (table 4). However, younger children were more likely to have an MC consultation than older children aged 10 to 14 years (OR:1.37 (95% CI 1.32 to 1.42) $P<0.005$).

Discussion

Summary

This large retrospective longitudinal analysis of MC cases presenting to primary care highlights a decline in the rate of primary care consultations between 2004 and 2013 by 50.0%. The overall consultation rate for children aged 0 to 14 years was 9.4 per 1,000 (95% CI 9.3 to 9.4), and the age groups with the highest consultation rates were the 1 to 4 and 5 to 9 year age groups (12.8 to 13.7 per 1,000). There was little variation between genders. In total, 0.8% of patients were referred to a secondary care dermatologist, and the number of referrals annually reduced by 74.4% from 2004 to 2013. 46.6% of consultations resulted in a prescription, with emollients and topical corticosteroids being the most common agents to be prescribed.

The matched cohort study demonstrated that children who have a primary care diagnosis of AE are more likely to have a future MC consultation than age-sex matched controls (OR:1.13 (95% CI 1.10 to 1.16) $P<0.005$).

Strengths and limitations

We extracted data from the CPRD database, which is the largest database of primary care consultations in the UK but is not inclusive of all UK general practices. CPRD data have been subjected to a number of validity assessments and been found to be representative of the UK population (17, 18). As with all studies reporting consultation rates of a condition using routinely collected data, this is subject to coding problems and under-ascertainment (19-25). The analysis does not determine causal relationships but describes associations within the data and although observational studies do not categorically identify 'cause and effect' they are important. By identifying associations between MC, age and AE this can provide evidence of the etiology of disease and can lead to further research to explore this further.

This study described children who had an MC diagnosis confirmed and correctly diagnosed by a primary care physician; therefore this will underestimate the true incidence of MC in the community. There is little evidence available of what the prevalence of MC in the community may be, however as these children do not present to primary care then it can be assumed they are successfully managing the condition.

MC is a self-limiting condition and the most recent Cochrane review of treatments for cutaneous MC (2009) recommends that the condition should be left to resolve naturally (26). In consultations where MC is discussed as a secondary problem, and / or where clinicians are providing only verbal advice and not prescribing treatments, a Read-code for MC may not be entered. Therefore, our estimates are likely to represent an underestimate of the true incidence of MC consultations. There are also limitations in the correct coding of data held within CPRD (27) and the use of appropriate coding and confirming a correct diagnosis of MC is unknown. However by only including "up to standard" data the impact of this source of error has been minimised.

Prescriptions are generally well-coded in CPRD, but they are not directly linked to a diagnosis (only linked by consultation). Therefore, it is possible that the medications identified as being linked to MC consultations may actually relate to alternative diagnoses. Given the most commonly prescribed medications were emollients and topical corticosteroids, associated AE is likely to be the reason for some of the prescribing.

Comparison with existing literature

There are few epidemiological studies of MC conducted in the United Kingdom (UK). Two previous studies extracted routinely collected data on consultation rates of MC from a sentinel network of general practices (Weekly Returns of the Royal College of General Practitioners) in England and Wales; one from 1994 to 2003 (7) and the other from 2006 (6). Both studies found similar consultation rates, the greatest being in children aged 1 to 4 years (15.0 to 17.2 per 1,000) (7). Neither of these studies presented data for children aged 5 to 9 or 10 to 14, instead merging these into a 5 to 14 group. Our data highlights that when data is analysed in these groups consultations of MC are greatest in the 1 to 4 and 5 to 9 year age groups (12.8 to 13.7 per 1,000). Our data also provides a higher rate of consultations in 2004 than that given by Pannell in 2003 (7), this may be due to our study using more specific and narrower age ranges than those used in previous studies.

Annual trends of MC consultations in the UK were previously reported for the period 1994 to 2003 (7), where the consultation rate rose by 38.5% from 1994 to 1998 (8 per 1,000 to 13 per 1,000). The rates remained constant until 2002 until there was a drop in the rate during 2003. Our data from 2004 show a continuation of this decline. The decrease in primary care consultations for MC may be caused by the increased availability of health care information online (28) which has resulted in a reduction in parents presenting to primary care if

provided with adequate information on health websites (29). A second consideration for the decreasing trends in consultations for MC may be due to true changes in the incidence of infectious disease in developed countries (30). Reasons for reductions in some infectious diseases during the past century may be due to improved sanitary conditions, less extreme poverty and a decrease in large numbers of children living within one household. For MC, limited close contact to other children with the condition and improved sanitary conditions could significantly reduce the opportunity for transmission between children and the overall prevalence of the condition within the population.

AE is associated with abnormalities in immune regulation, and patients with AE are known to be more susceptible to a range of cutaneous infections (31). Our study is the first to prospectively follow a retrospective cohort in order to determine whether children with a diagnosis of AE have an increased risk of subsequent MC. We were able to demonstrate that children with AE are 13% more likely to develop MC than children who do not have this diagnosis. Most previous research has also demonstrated an association between AE and MC. A case-control study of children aged 5 years and under identified following outpatient visits in North America found that those with a diagnosis of MC were more likely to have a either a current or previous AE diagnosis when compared to controls (15). Another case-control study identified children with MC and compared the prevalence of AE with that of a previous national cross-sectional study. They found a prevalence of 18.2% in the MC cohort and 5% in the national survey (14). Other studies have found a prevalence of AE in children with MC of 24% (32) to 43% (11) by reviewing the case notes of children attending outpatient clinics. However, one study, in a paediatric outpatient clinic in Brazil, found no difference in the frequency of MC in children with and without AE (12).

The association we describe between children with AE who develop MC may be less than what might have been expected from clinical impressions and described in the literature. One reason may be due to coding issues for both conditions which may under report the number of children who have a recorded clinical diagnosis of both MC and AE. Improved management of AE could also have contributed to the lower than expected effect size of the association, optimal eczema management has provided rapid improvement in skin barrier function (33), thus reducing the future development of other skin conditions such as MC.

Implications for research and/or practice

General practice consultations that include a code for MC are common but have reduced by 50% since 2004. The highest consultation rates are in children aged 1 to 4 and 5 to 9 years. MC is often accompanied by AE and we have demonstrated that children who have a primary care diagnosis of AE are more likely to have a subsequent MC consultation. The mechanisms involved in the development of MC, and the reasons for the increased risk associated with AE, require further understanding.

How this fits in

Molluscum contagiosum (MC) is a common skin condition in children, however recent consultation rates have not been describe in the UK. It is common that children with MC also present with atopic eczema (AE) to primary and secondary care, however the risk of developing MC in children with a history of AE is not clear. We found largest rate in consultations of MC is in children aged 1 to 4 and 5 to 9 years (12.8 to 13.7 per 1,000) and consultation rates have decreased by 50.0% for MC, from 2004 to 2013. We found evidence of an increased likelihood of subsequent MC in children with a primary care diagnosis of AE.

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Ethical Approval

This study was approved by the independent scientific advisory committee (ISAC) for the UK Medicines and Healthcare Products Regulatory Agency (MHRA) database research (Ref: 14_058R).

Competing Interests

The authors have declared no competing interests.

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Tables.

Table 1: Consultation rate per 1,000 registered population, 2004-13, by age group and gender.

Age Group	Events		Population		Consultation rate per 1,000					
	M	F	M	F	M	LCI	UCI	F	LCI	UCI
Under 1	547	411	282,744	268,564	1.9	1.8	2.1	1.5	1.4	1.7
1 to 4	17,296	16,237	1,316,034	1,252,919	13.1	12.9	13.3	13.0	12.8	13.2
5 to 9	20,151	20,600	1,552,618	1,479,532	13.0	12.8	13.2	13.9	13.7	14.1
10 to 14	7,001	6,772	1,587,807	1,505,629	4.4	4.3	4.5	4.5	4.4	4.6
Total	44,995	44,020	4,739,203	4,506,644	9.5	9.4	9.6	9.8	9.7	9.9

Table 2: Treatments prescribed during a patients consultation for MC (where prescribed in over 1% of cases).

BNF sub-section heading	Freq.	%
Emollient & Barrier Preparations	14,645	20.5
Topical Corticosteroids	14,496	20.3
Anti-Infective Skin Preparations	13,075	18.3
Antibacterial Drugs	10,647	14.9
Antihistamines, Hyposensitive & Allergic Emergencies	3,097	4.3
Preparations For Warts And Calluses	1,727	2.4
Bronchodilators	1,635	2.3
Skin Cleansers, Antiseptics & Wound prep	1,412	2.0
Analgesics	1,129	1.6
Anti-Infective Eye Preparations	938	1.3
Corticosteroids	829	1.2
Top Local Anaesthetics & Antipruritic	750	1.1

Table 3: Consultations for AE per patient during period 2004-13 and time to MC consultation (for those who consulted for MC).

a) Number of consultations for AE per patient during period 2004-13			
Number of consultations	Frequency	Percent	
1	222,710	58.9	
3	73,270	19.4	
4	32,523	8.6	
5 or more	49,382	13.1	
Range	1	to	105
Median	1	Q_1 to Q_3	1 to 3
b) Time between AE and MC consultation in cases of AE who also consulted for MC			
Time from AE>MC consultations	Frequency	Percent	
Initial AE \geq 30 days prior to MC consultation	15,016	65.2	
Initial AE consultation during or after an MC consultation	7,793	33.8	
Initial AE consultation < 30 to 1 day prior to MC consultation	240	1.0	
Total children who consulted for AE and MC	23,049	100	

Table 4: Odds ratio (OR) of MC consultation in patients with previous AE diagnosis.

a) Association of developing MC following previous AE diagnosis						
Cases		Controls		OR	95% CI	P
No MC	MC	No MC	MC			
362,869	15,016	364,599	13,289	1.13	1.11 to 1.16	<0.005
b) Multivariate analysis of association of developing MC within the following groups of patients with AE:						
i) Corticosteroids potency						
	Corticosteroid strength			OR	95% CI	P
	Mild			Ref		
	Moderate			0.37	0.10 to 1.50	0.16
	Potent or very potent			0.88	0.73 to 1.06	0.17
ii) Age at initial AE diagnosis						
	Age group (years)			OR	95% CI	P
	Under 1			Ref		
	1 to 4			1.37	1.32 to 1.42	<0.005
	5 to 9			1.04	0.99 to 1.10	0.07
	10 to 14			0.25	0.23 to 0.27	<0.005
iii) AE diagnosis (Supplementary table 2)						
	Analysis			OR	95% CI	P
	Primary AE diagnosis			Ref		
	Secondary AE diagnosis			0.89	0.83 to 0.94	<0.005

Note: i), ii) and iii) are independent variables in a single multiple logistic regression model.

Figures.

Figure 1: Data extraction flow chart

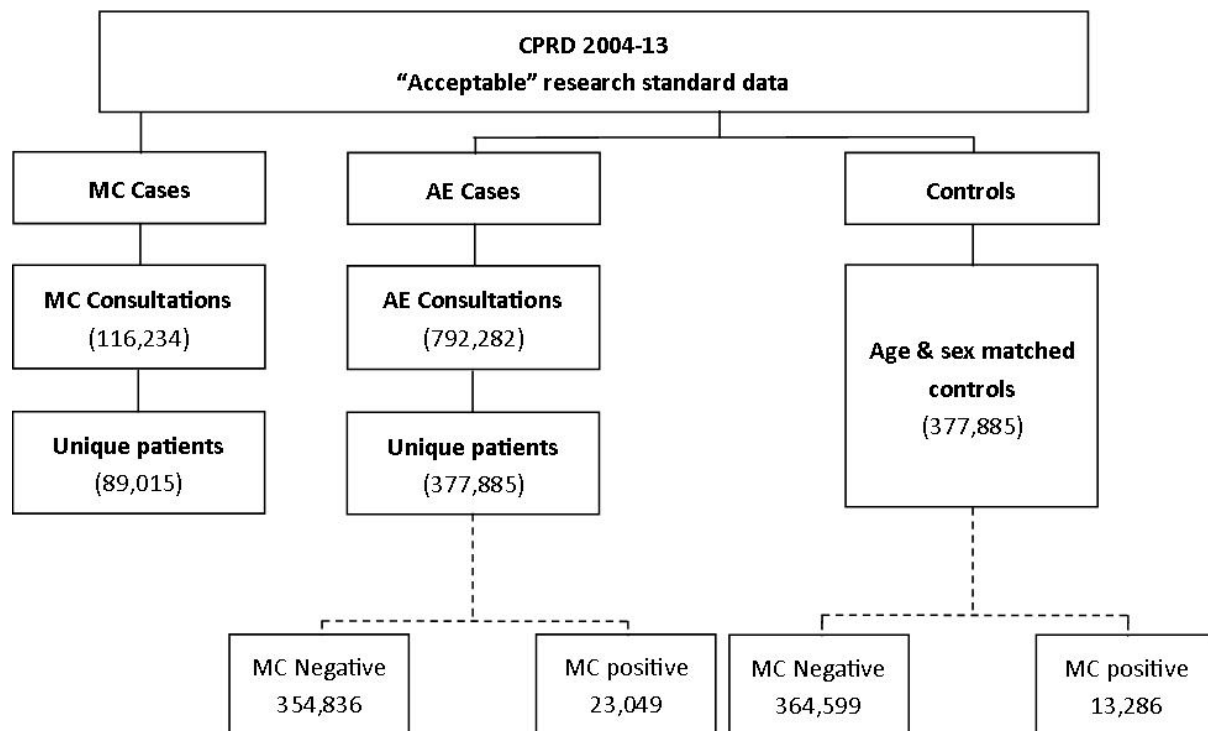


Figure 2: Consultation rate per 1,000 registered population, males and females, by year and age group.

